Targeted MicroRNA Interference Promotes Postnatal Cardiac Cell Cycle Re-Entry.

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Public Summary:
Mammalian heart cells undergo a marked reduction in proliferative activity shortly after birth, and thereafter grow predominantly by hypertrophy. Our understanding of the molecular mechanisms underlying cardiac maturation and senescence is based largely on studies at the whole-heart level. Here, we investigate the molecular basis of the acquired quiescence of purified neonatal and adult cardiomyocytes, and use microRNA interference as a novel strategy to promote cardiomyocyte cell cycle re-entry. Expression of cyclins and cyclin-dependent kinases (CDKs) and positive modulators were down-regulated, while CDK inhibitors and negative cell cycle modulators were up-regulated during postnatal maturation of cardiomyocytes. The expression pattern of microRNAs also changed dramatically, including increases in miR-29a, miR-30a and miR-141. Treatment of neonatal cardiomyocytes with miRNA inhibitors anti-miR-29a, anti-miR-30a, and antimiR-141 resulted in more cycling cells and enhanced expression of Cyclin A2 (CCNA2). Thus, targeted microRNA interference can reactivate postnatal cardiomyocyte proliferation.

Scientific Abstract:
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